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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/681,199	KERE ET AL.	
	Examiner	Art Unit	
	Jeanine A. Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *10-21,24 and 26-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,22,23,25 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed March 14, 2006. Currently, claims 1-34 are pending. Claims 10-21, 24, 26-33 have been withdrawn as drawn to non-elected subject matter.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

3. Any objections and rejections not reiterated below are hereby withdrawn.

   a. The Statutory Double Patenting Rejection has been withdrawn in view of the abandonment of 10/364,505.

   b. The 102 rejections over Brennan have been withdrawn in view of the amendment of Claim to require "the complement."

Maintained Rejections

Election/Restrictions

1. Applicant's election with traverse of Group I, Claims 1-9, 22-23, 25, SEQ ID NO: 1 in the paper filed June 22, 2005 and August 5, 2005 is acknowledged.

The response asserts that there is no undue burden to examine and consider all the claims. This argument has been thoroughly reviewed, but is not found persuasive because the claims are drawn to numerous groups of patentably distinct claims, as exemplified by the separate classification. Further, the claims are drawn to numerous polymorphisms which require separate consideration and search. Each polymorphism requires both a sequence search, a text search. Art on one particular polymorphism

would not necessarily be art on a separate polymorphism, thus, multiple searches would be required to examine the entire application as a whole.

Claims 10-21, 24, 26-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement.

The requirement is still deemed proper and is therefore made FINAL.

Priority

2. This application claims priority to 10/364,505, filed February 12, 2003 and provisional application 60/355,782, filed February 12, 2002 and application PCT/FI03/001100, Filed February 12, 2003.

Drawings

3. The drawings are acceptable.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-8, 22-23, 25, 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated and purified DYXC1 polynucleotide consisting of SEQ ID NO: 1 or the complement thereof; a homolog of SEQ ID NO: 1 with at least 79% homologous to SEQ ID NO:-encoded polypeptide. The claims are also directed to a nucleic acid able to hybridize to SEQ ID NO: under high stringency conditions provided in Claim 1.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...' required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. The claims are directed to homologs of DYXC1. The specification teaches human, mouse, pan troglodytes (SEQ ID NO: 13), gorilla (SEQ ID NO: 15), Pongo pygmaeus (SEQ ID NO: 17) and Pan paniscus (SEQ ID NO: 19) nucleic acids. Theses sequences minimally have 55% identity with the human DYXC1 nucleic acid. The claims encompasses full-length genes and cDNAs that are not described. The genus of homologs of DYXC1 encompasses dog, cat, opossum, squirrel, insect, earthworm, for example. There is substantial variability among the species of DNAs encompassed within the scope of the claims as evidenced by the variation between closely related primates. Weighing all factors, 1) partial structure of the DNAs that comprise SEQ ID NO: 29, 2) breadth of the claims as reading on genes yet to be discovered in 3) the lack of correlation between the structure and function of the genes; in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of DNAs which are homologs of SEQ ID NO: 1. There does not appear to be any function described for DYXC1 which would allow the skilled artisan to ascertain whether they have a DYXC1 homolog. There is no assay which would provide support for identification of homologs of DYXC1. Accordingly, Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus.

With respect to claims which encompass allelic variations. As provided in Example 11, no common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 1 alone is insufficient to describe the genus. There is no description of the mutational sites that exist in nature and there is no description of how the structure of SEQ ID NO: 1 relates to the structure of any strictly neutral alleles. Variants, as claimed, would encompass not only SNPs, but would also encompass deletions, insertions, splice variants and other variations within the nucleic acid sequence. The '505 application disclosed 5 specific SNPs within the DYXC1 nucleic acid. The instant application teaches 8 SNPs within the DYXC1 nucleic acid. The general knowledge in the art concerning variants does not provide any indication of how the structure of one allele is representative of unknown alleles. The nature of alleles is such that they are variant structures, and in the present state of the art the structure of one does not provide guidance to the structure of others. The common attributes are not described. One of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claim. Marino et al. (E. J. Human Genetics, Vol. 13, pages 491-499, 2005) teaches an additional 3 variants within the DYX1C1 gene. The disclosed variants of the instant application are not representative of the later disclosed

variants of Marino. At the time the invention was made, the disclosed variants were not representative of the entire genus of variants encompassed by the claims.

Finally, the claims are drawn to hybridization language (see Claims 4-5). Example 9 of the written description guidelines states that a structure function relationship with hybridization language may satisfy the written description guidelines. The instant claims do not provide a structure function relationship with hybridization language. Therefore, the hybridization language would encompass sequences from other species, mutated fragment sequences, allelic variants, splice variants, genomic sequences and so forth.

Accordingly, Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus.

Response to Arguments

The response traverses the rejection. The response asserts the claims have been amended to overcome the rejection. This argument has been considered but is not convincing because the claim remains drawn to embodiments in which applicants were not in possession of at the time of filing. Specifically, as provided in the Written Description Guidelines, the structure function relationship required for hybridization language has not been presented. The final clause in the instant claim is "wherein said nucleic acid is genetically linked to dyslexia" however the specification fails to setforth a particular assay or test to determine the function. Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-9, 22-23, 25, 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated and purified DYXC1 nucleic acid comprising SEQ ID NO: 1, 13, 15, 17, 19, and the complements thereof, does not reasonably provide enablement for a nucleic acid homolog, variant, fragment or nucleic acid which hybridizes to SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

<u>The nature of the invention and breadth of claims</u>

The claims are drawn to an isolated and purified DYXC1 polynucleotide consisting of SEQ ID NO: 1 or the complement thereof; a homolog of SEQ ID NO: 1 with at least 79% homologous to SEQ ID NO:-encoded polypeptide. The claims are also directed to a nucleic acid able to hybridize to SEQ ID NO: under high stringency conditions provided in Claim 1.

The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

The art teaches genetic variations and associations are often irreproducible. Hirschhorn et al. (Genetics in Medicine. Vol. 4, No. 2, pages 45-61, March 2002) teaches that most reported associations are not robust. Of the 166 associations studied three or more times, only 6 have been consistently replicated. Hirschhorn *et al.* suggest a number of reasons for the irreproducibility of studies, suggesting population stratification, linkage disequilibrium, gene-gene or gene-environment interactions, and weak genetic effects and lack of power are possible factors that lead to such irreproducibility. Hirschhorn *et al.* caution that the current irreproducibility of most association studies should raise a cautionary alarm when considering their use as diagnostics and prognostics (p. 60, Col. 2). Thus, Hirschhorn cautions in drawing conclusions from a single report of an association between a genetic variant and disease susceptibility.

Additionally, Ioannidis (Nature Genetics, Vol. 29, pages 306-309, November 2001) teaches that the results of the first study correlate only modestly with subsequent research on the same association (abstract). Ioannidis teaches that both bias and

genuine population diversity might explain why early association studies tend to overestimate the disease protection or predisposition conferred by a genetic polymorphism (abstract).

The art teaches that presence of SNPs in the same gene does not indicate that each of the genes is associated with the same diseases. Meyer et al. (PG Pub 2003/0092019), for example, teaches that SNPs in the CADPKL gene are not each associated with neuropsychiatric disorders such as schizophrenia. Specifically Meyer teaches that cadpkl5 and cadpkl6 are not associated with the disease, however cadpkl7 has a p-value of less than 0.05, therefore an association exists. Each of these polymorphisms are SNPs within the CADPKL gene, however, it is apparent that they are not all associated in the same manner with disease. Thus, Meyer exemplifies that the association of a single SNP in a gene does not indicate that all SNPs within the gene are associated with the disease.

The art teaches a family-based association study that does not support DYX1C1 on 15q21.3 as a candidate gene in developmental dyslexia. Marino et al. (E. J. Human Genetics, Vol. 13, pages 491-499, 2005) teaches 8 SNPs, three of which were suitable for genetic analysis. The analyses did not support the involvement of the DYX1C1 gene variants in this sample of dyslexics and their relatives. Marino states that "we were unable to replicate the original findings between DYX1C1 gene and developmental dyslexia, perhaps due to genetic heterogeneity. Mario states that haplotype analysis further increased the number of informative families (page 498, col. 1).

Scerri et al. (J. Med. Genet. Vol. 41, pages 853-857, 2004) teaches putative functional alleles of DYX1C1 are not associated with dyslexia susceptibility in a large sample of sibling pairs from the UK. Scerri teaches that only one of eight sequence variants showed nominally any significant association with any of the quantitative

measures. Scerri teaches that the DYX1C1 alleles previously associated with dyslexia are not associated with the trait in their sample. Scerri teaches that, like Wigg, the data of their study, that a biased transmission of the –3G/1249G haplotype children with poorer reading related skills (opposite finding to the original report by Taipale) (page 857, col. 1).

Wigg et al (Mol. Psychiatry, Vol. 9, pages 1111-1121, 2004) teaches support for EKN1 as the susceptibility locus for dyslexia on 15q21. Wigg teaches that EKN1, with unknown function in the linked region was identified via a translocation breakpoint. Wigg analyses several polymorphisms, however, only the 1249 polymorphism appears to be individually associated with dyslexia. Wigg further teaches haplotype analysis and that haplotype analysis increases the power of the analysis (page 1117, col. 2). Wigg teaches that the relevant DNA changes may be located in regulatory sequences, and the regions that must be screened may be quite large given that these regions have not been yet delineated (page 1120, col. 2). Further Wigg acknowledges that these are preliminary findings and further replication studies are necessary before definitive conclusions can be made (col. 1120, col. 2).

Guidance in the Specification and Working Examples

The specification teaches a DYXC1 nucleic acid sequence for human (SEQ ID NO: 1); mouse (SEQ ID NO: 4), pan troglodytes (SEQ ID NO: 13), gorilla (SEQ ID NO: 15), Pongo pygmaeus (SEQ ID NO: 17) and Pan paniscus (SEQ ID NO: 19). Further, the specification teaches 8 polymorphisms within DYXC1 nucleic acid of SEQ ID NO: 1. Table 1 illustrates the frequency of single nucleotide polymorphisms in dyslexic subjects and controls. Only two polymorphisms appear to show any association with dyslexia at a significant level. –3G to A and 1249 G-T. The guidance

provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied before the skilled artisan would be able to used the claimed invention as broadly as claimed.

While nucleic acids which may hybridize to the DYXC1 may be obtained through hybridization analysis. The skilled artisan would be unable to use these variant nucleic acids without further unpredictable and undue experimentation.

Given the lack of teachings in the art and the specification regarding the function of DYXC1, it is unclear how the skilled artisan would know they have obtained a DYXC1 homolog of a dog or cat nucleic acid, for example. The specification fails to provide any function for the claimed nucleic acid homologs. Further, the wide range of similarity between primates, for example, would not allow the skilled artisan to immediately recognize the presence of a DYXC1 nucleic acid.

With respect to variants of DYXC1, both the specification and the post-filing date art support that not all SNPs or variants are associated with dyslexia. The skilled artisan would not be appraised of how to use variant nucleic acids which are not associated with dyslexia. As seen in Table 1, -164; -2; 4; 271; 572; 1259 do not have a significant association with dyslexia. Similarly, the post filing date art supports that these polymorphisms and additional polymorphisms are not associated in a significant manner with dyslexia.

To use the claimed invention to the full scope of the instant claims would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art for determining the function of newly identified nucleic acids, for the skilled artisan to be able to practice the claimed invention as broadly as claimed, the skilled artisan would be required to perform additional and undue and unpredictable experimentation. Further, the prior art and the specification provides insufficient guidance to overcome the art recognized difficulties in assigning function to particular nucleic acids. Obtaining nucleic acids which hybridize to particular nucleic acids would be routine in the art, however, assigning the nucleic acids as DYXC1 nucleic acids or having a particular function that would enable the skilled artisan to use the nucleic acids would have been undue and unpredictable at the time the invention was made. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Response to Arguments

The response traverses the rejection. The response asserts the claims have been amended to overcome the rejection. This argument has been considered but is not convincing because the claim remains drawn to embodiments in which applicants had not enabled at the time of filing. As discussed in the rejection above, the skilled artisan would not know how to use any nucleic acid which hybridizes with SEQ ID NO: 1. As provided in the specification numerous allelic variations do not appear to be associated or linked to dyslexia. Therefore, it is undue experimentation to determine how the skilled artisan would use the claimed invention. Moreover, there is no structure function relationship provided in the instant specification which allows the skilled artisan to determine whether a nucleic acid is a homolog of SEQ ID NO: 1. Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by NIH-MGC (Genbank Accession Number BE972748, October 4, 2000).

NIH-MGC teaches a nucleic acid human cDNA clone EST. The nucleic acid is 100% identical to instant SEQ ID NO: 1 over 364 nucleotides. Nucleotides 686-1049 of the instant SEQ ID NO: 1 are 100% identical to nucleotides 1-364 of NIH-MGC (see

attached alignment)(limitations of Claims 1-3, 6). The nucleic acid is disclosed within a vector and host cell, namely DH10B and vector pDNR-LIB (limitations of Claims 7-8). Since the nucleic acid is 100% identical over 364 nucleotides, the nucleic acid would certainly hybridize under high stringency conditions to SEQ ID NO: 1 (limitations of Claims 1, 4, 5).

Response to Arguments

The response traverses the rejection. The response asserts the claims have been amended to no longer encompass fragments thereof. This argument has been considered but is not convincing because Claim 1 has been amended to include hybridization language. As provided in the original rejection, since the nucleic acid is 100% identical over 364 nucleotides, the nucleic acid would certainly hybridize under high stringency conditions to SEQ ID NO: 1. Thus for the reasons above and those already of record, the rejection is maintained.

7. Claims 1-6, 9 are rejected under 35 U.S.C. 102 (a) as being anticipated by Taipale et al. (Genbank Accession Number AF337549, February 2, 2002).

Taipale et al. teaches a nucleic acid EKN1 mRNA from human. Nucleotides 1-1263 of instant SEQ ID NO: 1 are 100% identical to nucleotides 369-1631 of Taipale (see attached alignment).

Response to Arguments

The response traverses the rejection. The response asserts the present application claims priority to US Provisional Application filed on February 12, 2002 and

thus Taipale is not available as prior art under 102(b). This argument has been considered but is not convincing because the rejection was made under 102(a) (see original rejection). Thus for the reasons above and those already of record, the rejection is maintained.

8. Claims 22-23, 25, and Newly added Claim 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Applied Biosystems Product Catalog (1993, pages 135-164).

It is noted that these claims contain a preamble which recites an intended use, however, it is also noted that this use does not confer patentable weight on the product claims since the preamble does not materially change what is present in the kit itself and thus represents an intended use of the kit (see MPEP 2111.02). Further, with regard to the limitation of Claim 25, that the kits contain instructions for using said, the inclusion of instructions is not considered to provide a patentable limitation on the claims. See In re Ngai, 367 F.3d 1336, 70 U.S.P.Q.2d 1862 (Fed. Cir. 2004)(holding that an inventor could not patent known kits by simply attaching new set of instructions to that product).

Applied Biosystems provides several products which are packaged for distribution, kits, which allow for detecting the presence of variant alleles of two or more genes. Applied Biosystems products for sale include: a DNA analysis system; software for genetic analysis; electrophoresis accessories including combs, alignment braces, glass plates, manuals; PRISM Ready reaction cycle sequencing kits; AmpliTaq Cycling

Sequencing Kits; DNA sequencing Neat reagents Dye primers; activated dyes, template purification kits; etc. Each of these products is capable of detecting the presence of variant alleles of two or more genes. Applied Biosystems teaches numerous computer programs which are sold with the DNA analysis system, for example. Specifically, DNA analysis system- Model 373 is a system which relies upon gel electrophoresis. Sizing, quantitation and sequencing data are automatically generated by GENESCAN or DNA sequence Analysis software. Applied Biosystems uses fluorescence technology for labeling DNA samples and allows products of all four reactions to be run in the same lane. The color-coded data is graphically represented and a corresponding report gives molecular sizes in base pairs and quantity by relative fluorescence amount (page 136). As seen on page 137, col. 1, DNA sequencing and GENESCAN software generate color-coded data with tremendous explanatory power. A tabular report gives band elution time, base pair size, and relative fluorescence amount. Therefore, the computer program associated with the Applied Biosystems system contains instructions which direct a processor to analyze data derived from the use of the labels, gel, electrophoretic machine, the power supply etc. The system specifically allows for detection of four labels which would enable detection of variant alleles in two or more genes, associated with two or more conditions, as required by the instant claims.

As decided at the Federal Circuit in May 2004, In re Ngai succinctly states that inventors are not "entitled to patent a known product by simply attaching a set of instructions to that product." As in Ngai, the only difference between the Applied

Biosystems system and the instant claims is the content of the instructions. Therefore, the different instructions provided in Claims 25 do not distinguish over the prior art.

Therefore, since Applied Biosystems teaches every limitation of the claims, Applied Biosystems anticipates the claimed invention.

Response to Arguments

The response traverses the rejection. The response asserts that the nowhere in ABP is there disclosed a compound that specifically detects the DYXC1 gene. This argument has been considered but is not convincing because the claim is not drawn to a compound that specifically detects the DYXC1 gene. The claim is drawn to a compound capable of detecting DYXC1 gene. Applied Biosystems products for sale include: a DNA analysis system; software for genetic analysis; electrophoresis accessories including combs, alignment braces, glass plates, manuals; PRISM Ready reaction cycle sequencing kits; AmpliTaq Cycling Sequencing Kits; DNA sequencing Neat reagents Dye primers; activated dyes, template purification kits; etc. Each of these products is capable of detecting the presence of variant alleles of two or more genes. The compound provided in the kit is not required to be a nucleic acid, nor a nucleic acid of any particular structure. The compound must only be capable of detecting the DYXC1 gene. Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 22-23, 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brennan (US Patent 5,474,796, December 12, 1995) in view of Ahern (The Scientist, Vol 9, No. 15, page 20, July 1995).

Brennan teaches oligonucleotides having 10 nucleotides each (10-mers). The oligonucleotides represent every possible permutation of the 10-mer oligonucleotide.

Brennan does not specifically teach placing the array with instructions into a kit.

However, Ahern teaches reagent kits offer scientists good return on investment. Ahern teaches kits save time and money because the kits already comes prepared.

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have modified the teachings of Brennan with the teachings of Ahern to incorporate the necessary reagents into a packaged kit. The ordinary artisan would have been motivated to have packaged the primers, probes, and reagents of Brennan into a kit, as taught by Ahern for the express purpose of saving time and money.

With regard to the limitation that the kits contain instructions, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit. See In re Ngai, 367 F.3d 1336, 70 U.S.P.Q.2d 1862 (Fed. Cir. 2004)(holding that an inventor could not patent known kits by simply attaching new set of instructions to that product).

Response to Arguments

The response traverses the rejection. The response asserts Brennan does not teach placing the array with instructions into a kit. Further Ahern discloses nothing about SEQ ID NO: 1. This argument has been considered but is not convincing because the claim is drawn to a compound capable of detecting DYXC1 gene. The 10-mer array of Brennan would be capable of detecting DYXC1 gene. Thus for the reasons above and those already of record, the rejection is maintained.

New Grounds of Rejection Necessitated by Amendment

New Matter

11. Claims 1-9, 22-23, 25, 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the amended claims, reference to "a homologue of a SEO ID No: I -encoded polypeptide. wherein said homologue is at least 79% homologous to a SEO ID No:I-encoded polypeptide." are included. The amendment proposes that the new claim language is supported by the specification. However, the specification does not describe or discuss "a homologue of a SEO ID No:I-encoded polypeptide wherein said homologue is at least 79% homologous to a SEO ID No:I-encoded polypeptide." Instead the specification describes "preferred homologs" have a sequence at least about 79% homologous with a nucleotide sequence of SEQ ID NO: 1. The percentage homologous to a nucleic acid sequence and an encoded protein sequence are not synonymous or equivalent. This description does not support a homolog of a SEO ID No: I -encoded polypeptide wherein said homologue is at least 79% homologous to a SEO ID No:I-encoded polypeptide. The concept of "a homologue of a SEO ID No: I -encoded polypeptide. wherein said homologue is at least 79% homologous to a SEO ID No:I-encoded polypeptide" does not appear to be part of the originally filed invention. Therefore, "a homologue of a SEO ID No: I -encoded polypeptide. wherein said homologue is at least 79% homologous to a SEO ID No:I-encoded polypeptide"

constitutes new matter. Applicant is required to cancel the new matter in the reply to this Office Action.

Conclusion

12. No claims allowable.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

J. Goldberg

Jeanine Goldberg
Primary Examiner
April 20, 2006